

Fig. 1

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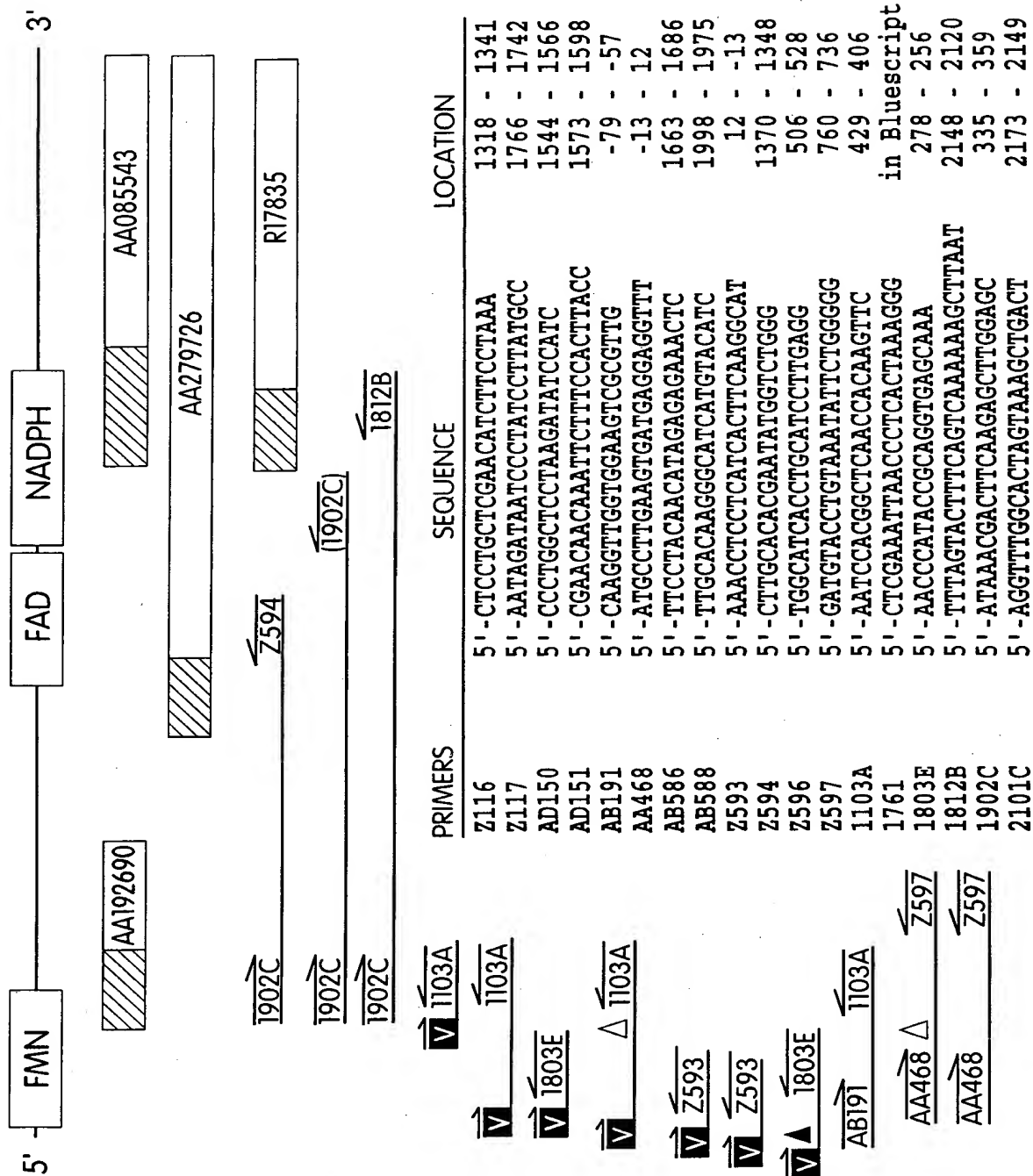


Fig. 2

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CAAGTTGGTGAAGTCCGTTGTGAGGTTCTGTCGGGCTGGCGCGGCTGTTTCACTGTTACATGCCTTGAAGTG
1 ATGAGGAGTTTCTGTTACTATATGCTACACAGCAGGAGCAGGCAAGCCATCGCAGAGAAATGTGTGAGCAAGCTGTGGTACATGATTTTTCAGATCTTCACTGTATTAGTGAA
M R R F L L L Y A T Q Q G Q A K A I A E M C E Q A V V H G F S A D L H C I S E 40
121 TCCGATAGTATGACCTTAAACCGAAACAGCTCTCTGTTGTTGTTTACACGGGACCGGAGACCCACACACAGCCCGCAAGTTGTTAAGGAAATACAGAACCAACA
S D K Y D L K T E T A P L V V V S T T G T G D P P D T A R K F V K E I Q N Q T 80
241 CTGCGGTTGATTTCTTCTCACTCGGTATGGGTACTGGTTCAGAAATACACCTACTTTTGCATGGGGGGAAGATAATTGATAAACGACTTCAAGAGCTTGGGAGCC
L P V D F F A H L R Y G L L G L G D S E Y T Y F C N G G K I I D K R L Q E L G A 120
361 CGGCATTCTATGACACTGGACATGCAGATGACTGTGTAGCTTGTGAGTGGCGTGGATGCTGGACTCTGGCCAGCCCTCAGAAAGCATTTTAGGTCAAGCAGAGGACAA
R H F Y D T G H A D D C V G L E L V V E P W I A G L W P A L R K H F R S S R G Q 160
481 GAGGAGATAAGTGGCGCACTCCGGTGGCATCACCTGCATCCTTGAGGACAGACCTTGTGAAGTCAAGCTGCTACATTTGAATCTCAAGTCGAGCTTCTGAGATTCGATTCAGGA
E E I S G A L P V A S P A S L R T D L V K S E L L H I E S Q V E L L R F D D S G 200
601 AGAAGGATCTGAGTTTGAAGCAAAATGCAGTGAACCAATCCAAATGTTGTAATGAAGACTTTGAGTCTCCTCACTTACCCGTTGGTACCCCACTCTCAAGCCTCTCTG
R K D S E V L K Q N A V N S N Q S N V V I E D F E S S L T R S V P P L S Q A S L 240
721 AATATTCCTGGTTACCCCGAGATATTTACAGGTACATCTGCAGAGTCTCTTGCCAGGAGAAACCAAGTATCTGTGACTTCAGCAGATCCAGTTTTCAGTGCCCAATTTCAAAG
N I P G L P P E Y L Q V H L Q E S L G Q E E S Q V S V T S A D P V F Q V P I S K 280
841 GCAGTCACTTACTAGATGATGCCATFAAAACCACTGCTGCTAGATTTGACATTTCAAATACAGACTTTTCTATCAGCTGGAGATGCTTCAGGCTGATCTGCCCTAACAGT
A V Q L T T N D A I K T T L L V E L D I S N T D F S Y Q P G D A F S V I C P N S 320
961 GATTCAGGTACAAGCTACTCCAAGACTGCAGCTTGAAGATAAAGAGAGCACTCGCTCTTTTGAATAAAGCAGACACAAAGAAAGAGGAGTACCTTACCCCGCATATA
D S E V Q S L L Q R L Q L E D K R E H C V L L K I K A D T K K G A T L P Q H I 360
1081 CCTGCGGATGTTCTCTCCAGTTCATTTTACCTGGTGTCTTGAATCCGAGCAATTCCTAAAAGGCAATTTTGGAGCCCTTGTGGACTATACAGTGACAGTGTGTAAGGCGCAGG
P A G C S L Q F I F T W C L E I R A I P K K A F L R A L V D Y T S D S A E K R R 400
1201 CTACAGGAGCTGTGCAGTAACAGGGGAGCCGATTAAGCCGTTTGTACGAGATGCCCTGCTGTTGGATCTCCTCCTCGCTTCCCTTCTTGGCAGCCACCACTCAGTCTC
L Q E L C S K Q G A A D Y S R F V R D A C A C L L L D L L L A F P S C Q P P L S L 440

Fig. 3-1

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[illegible]

Fig. 3-2

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Fig. 3-3

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1321 CTGTCGAACATCTTCCCTAAACTTCAACCCAGACCATTATTCCTGTGCAAGCTCAAGTTTATTTACCCAGGAAGCTCCATTTTGTCTTCAACATTTGTGGAATTTCTGTCTACTGCCACA
L L E H L P K L Q P R P Y S C A S S L F H P G K L H F V F N I V E F L S T A T 480

1441 ACAGAGGTTCTGCGAAGGAGTATGTACAGCTGGCTGGCTTGTGGTCTTCAAGTTCTTCAGCCAAACATACATGTCATCCCATGAACACAGCGGGAAGCCCTGGCTCCTAAGATA
T E V L R K G V C T G W L A L L V A S V L Q P N I H A S H E D S G K A L A P K I 520

1561 TCCATCTCTCTCGAACAACAATTTCTTCCACTTACCAGATGACCCCTCAATCCCATCAATATGTTGGTCCAGGAACCGGCATAGCCCGTTTATTTGGTTCCTTACAACATAGAGAG
S I S P R T T N S F H L P D D P S I P I I M V G P G T G I A P F I G F L Q H R E 560

1681 AAATCCAAAGAACACACCAGATGGAATTTTGGACAAATGTGGTGTGGTCCAGCATAGGATAGGATATCTATTCAGAAAAGAGGTCAGACATTTCTTTAAGCATGGG
K L Q E Q H P D G N F G A M W L F F G C R H K D R D Y L F R K E L R H F L K H G 600

1801 ATCTTAATCTCTAAAGTTTCTTCTCAAGATGCTCTCTGTTGGGAGGAGGAGCCCAAGCAAGTATGTACAGCAACATCCAGCTTCATGCCCAGAGGTGGCGAGAAATCCTC
I L T H L K V S F S R D A P V G E E A P A K Y V Q D N I Q L H G Q Q V A R I L 640

1921 CTCAGGAGAACGGCCATATTTATGTGTGGAGATGCAAGAATATGGCAAGATGTACATGATGCCCTTGTGCAATAATAACAAAGAGGTTGAGATTGAAAACTAGAACGAATG
L Q E N G H I Y V C G D A K N M A K D V H D A L V Q I I S K E V G V E K L E A M 680

2041 AAAACCTGGCCACTTTAAAGAGAAACCGCTACCTTCAGGATATTTGGTCATATAAACAGAAATTAAGAAAGAGGATTAAGCTTTTGTGACTGAAAGTAAAGTCAGCTTTAC
K T L A T L K E E K R Y L Q D I W S ***

2161 TAGTGCCAAACCTTTAAATTTCAAAGAAATTTCTTCAACATTTCTTGAAGACATGGAGTGGAGATTGGATCATTTAAACAATAAACAACCTTCTCTGATTTGATTTTACGTATC
2281 TTCTATCTACGCCCTTCTGTGCTGTGACTCTCCCAATTTGCCCTGTTCCTGAGCTTCTGAGCTAAAGCAGCCTTCAGTCCCTATCAGCGCTCTCTTACTTCCAGAGAACT
2401 TCACAGAGACTCTGTCTCTCCATGCAAGGCTTCTGAAATAGGGAGACTGACTGAGTAGCTCATTTCTGTGACTTACAGTGCCAAACATTTAAAGATATGAAATGATTTATTTTA
2521 TATGATGTATACCCATAAGAAATGCTCATATTAATGCTACTTAAATPACACATGTAGACATATCTGTTATATGTTTATGTAACATCAAAATGGTTATTTGTTACTAAAGTATATTTCTG
2641 ATAAAAATATTTTAGGATAATTCCTACAGAGGATTTATTTTATGATGCTGGAAATATGAATGATTTTAAATTTCACTCTGGGATATGGAATTTATCTATCACCATTACTTTT
2761 TTTTAAGTCACAAATTTGGACATTTTGGACATTTTGGACATTTTACAGTACCATGATTTTAAAGAGATACAACTTTTATTTTACCTCTCTCTTTTATTTCTGCTGCTT
2881 GGCACATTTTGTGATTTTCCCAATTTTGTCTCCATGATACCACTCAAGAGTGTGCTGGAACCTAAATACTGACTTTAGTATCTCTGGAATTTTAGATTTCCCGAGTGTCTAAT
3001 TCCTCTGTATATTTGGACAAACAAATGTTATGATAATCTTCTCCACTGTTCTAATAATATGTTATTTTATTTGATGCTTGGGATTTTAAACATCTCTGTGTAAGGCTTT
3121 TGATCCTTTTGAAATTAAGATCTGAAGAAATGGCATATCTTAAAAAATAAAAAA

Fig. 3-4

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HsMTRR	-----	
CeMTRR	-----	
HsCPR	MGDSHVDTSSTVSEAVAEVSLFSMTDMILFSLIVGLLTYWFLFRKKKEE	50
	FMN	
HsMTRR	-----MRRFLLLYATQOQQAIAEEMCE	24
CeMTRR	-----MTDFLIAFGSQTGQAETIAKSLKE	24
HsCPR	VPEFTKIQTLTSSVRESSFVEKMKKTGRNIIVFYGSQTGTAEFANRLSK	100
 * * * * .	
	FMN	
HsMTRR	QAVVHGFSADLHCISESDK-YDLKT-----ETAPLVVVVSTTGTGDPP	66
CeMTRR	KAELIGLTPRLHALDENEEKFNLE-----EKLC-AIVVSSTGDGDAP	66
HsCPR	DAHRYG---MRGMSADPEEYDLADLSSLPEIDNALVVFCMATYGEDPT	146
	* * . . . * * * *	
	FMN	
HsMTRR	DTARKFVKEIQNTLPVDFFAHLRYGLLGLGDSEYTYFCNGGKIIDKRLQ	116
CeMTRR	DNCARFVRRINRNSLENEYLNLDYVLLGLGDSNYSSYQTIIPRKIDKQLT	116
HsCPR	DNAQDFYDWLQETDVD---LSGVKFAVFGLGNKTYEHFNAMGKYVDKRLE	193
	* * . . . * * * . . . * * *	
HsMTRR	ELGARHFYDTGHADDCVGLLELVVEPWIALGLWPALRKHFRRSSRGQEEISGA	166
CeMTRR	ALGANRLFDRAEADDQVGLLEVEPWIEKFFATLASRFDISADKMN----	162
HsCPR	QLGAQRIFELGLGDDDGNDLEEDFITWREQFWPAVCEHF-----GV	233
	*** . . . ** * * * . . *	
HsMTRR	LPVASPASLRITDLVKSELLHIESQVELL--RFDDSGRKDSEVLKQNAVNS	214
CeMTRR	-AITESSNLKLNQVKTE----EEKKALLQKRIEEDSDEGRGRVIGID-	206
HsCPR	EATGEESSIRQYEL-----VVHTDIDAQVYMGMGRLLKSYEN	271
	
HsMTRR	NQSNVVIEDF---ESSLTRSVPLS-QASLNIPGLPPEYLQVHLQESLGQ	260
CeMTRR	---MLIPEHYDYPEISLLKGSQTLSDENLRVPIAPQPPFIVSSVSNRKLP	253
HsCPR	QKP-----PFD-----AKNPFLAAVTTNRKLN	293
	
HsMTRR	EESQVS-----VTSADPVFQVPISKAVQLTT--NDAIKTTLLVELDIS	301
CeMTRR	EDTKLEWQNLCKMPGVVTKPFEVLVVSAEFVTDPFSSKKIKTKRMITVDFG	303
HsCPR	QGTE-----RHLMHLELD	306
	
HsMTRR	N--TDFSYQPGDAFSVICPNSDSEVQSLLQR-LQLEDKREHCVLLKIKAD	348
CeMTRR	DHAAELQYEPGDALFYFCVNPALVNFILKRCGVLDIADQOCEL-SINPK	352
HsCPR	ISDSKIRYESGDHVAVYPANDSALVNQLGK---ILGADLD--VMSLNNL	351
	. * . ** * * *	
HsMTRR	TKKKGATLPQHIPAGCSLQFIFTWCLEIRAIKKAFLRALVDYTSDSA EK	398
CeMTRR	TEKINAQIPGHVHKITTLRHMFTTCLDIRRAPGRPLIRVLAESTSDPNEK	402
HsCPR	DEESNKKHP--FPCPTSRYRTALTYLDITNPPRTNVLYELAQYASEPSEQ	399
	* . . . * * * * . . . * .	

Fig. 4-1

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HsMTRR	RRLQEL--CSKQGAADYSRFVRDACACLLDLLLAFPPSCQPPLSLLLEHLP	446
CeMTRR	RRLLEL--CSAQGMKDFDTDFVRTPGLSLADMLFAFPNVKPPVDRLIELLP	450
HsCPR	ELLRKMASSSGEGKELYLSWVVEARRHILAILQDCPSLRPPIDHLCCELLP	449
	* . * . * . . * . . * * * * *	
	FAD FAD FAD	
HsMTRR	KLQPRPYSCASSSLFHPGKLHFVFNIVEFLSTATTEVLRKGVCTGWLALL	496
CeMTRR	RLIPRPYSMSS---YENRKARLIYSEMEFPATDGRRHSRKGLATDWLNSL	497
HsCPR	RLQARYYSIASSSKVHPNSVHICAVVVEYETKAGR--INKGVATNWL---	494
	. * * * * . * . . * * * * *	
HsMTRR	VASVLQPNIHASHEDSGKALAPKISISPRTTNSFHLP-----DDPSIP	539
CeMTRR	R-----IGDKVQVLGKEPARFRLPPLGMTKNSAGKLP	529
HsCPR	RAKE-----PVGENGGRALVPMFVRKSQFRLPFK-----ATTP	527
	* *	
	NADPH	
HsMTRR	IIMVGPGTGIAPFIGFLQHREKLQEHPDGNFGAMW-LFFGCRHKDRDYL	588
CeMTRR	LLMVGPGTGVSVFLSFLHFLRKLKQDSPSDFVDVPRVLFFGCRDSSVDAI	579
HsCPR	VIMVGPGTGVAPFIGFIQERAWLRQQGKE---VGETLLYYGCRRSDEDYL	574
	..*****. * . * . * .. * .. * .	
	NADPH NADPH	
HsMTRR	FRKELRHFLKHGILTHLKVFSRDPVGEAAEAPAKYVQDNIQLHGQQVAR	638
CeMTRR	YMSELEMFVSEGILTDLIICESEQ-----KGERVQDGLRKYLDKVLP	621
HsCPR	YREELAQFHRDGALTQLNVAFSRE-----QSHKVYVQHLLKQDREHLWK	618
	. * * * * * * * * * * * * *	
	NADPH	
HsMTRR	ILLQE-NGHIYVCGDAKNMAKDVHDLVQIISKEVGVEKLEAMKTLATLK	687
CeMTRR	FLTASTESKIFICGDAKGMSKDVWQCFSDIVASDQGIPDLEAKKKLMDLK	671
HsCPR	LI--EGGAHIYVCGDARNMARDVQNTFYDIVAELGAMEHAQAVDYIKKLM	666
	. * ..*****. * .. * . * .. * . *	
	NADPH/FAD	
HsMTRR	EEKRYLQDIWS	698
CeMTRR	KSDQYIEDVWG	682
HsCPR	TKGRYSLDVWS	677
	* * *	

Fig. 4-2

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HsMTRR	-----	
CeMTRR	-----	
HsCPR	MGDSHVDTSSSTVSEAVAEVSLFSMTDMILFSLIVGLLTYWFLFRKKKEE	50
	FMN	
HsMTRR	-----MRRFLLLYATQOQQAIAEEMCE	24
CeMTRR	-----MTDFLIAFGSQTGQAETIAKSLKE	24
HsCPR	VPEFTKIQTLTSSVRESSFVEKMKKTGRNIIVFYGSQTGTAEFANRLSK	100
 * * * * .	
	FMN	
HsMTRR	QAVVHGFSADLHCISESDK-YDLKT-----ETAPLVVVVSTTGTGDPP	66
CeMTRR	KAELIGLTPRLHALDENEEKFNLE-----EKLC-AIVVSSTGDGDAP	66
HsCPR	DAHRYG----MRGMSADPEEYDLADLSSLPEIDNALVVFCMATYGEDPT	146
	* * * * * *	
	FMN	
HsMTRR	DTARKFVKEIQNTLPVDFFAHLRYGLLGLGDSEYTYFCNGGKIIDKRLQ	116
CeMTRR	DNCARFVRRINRNSLENEYLNLDYVLLGLGDSNYSSYQTIPIRKIDKQLT	116
HsCPR	DNAQDFYDWLQETDVD---LSGVKFAVFGLGNKTYEHFNAMGKYVDKRLE	193
	* * * * * * . * * *	
HsMTRR	ELGARHFYDTGHADDCVGLLELVVEPWIALGLWPALRKHFSSRGQEEISGA	166
CeMTRR	ALGANRLFDRAEADDQVGLELEVEPWIEKFFATLASRFDISADKMN----	162
HsCPR	QLGAQRIFELGLGDDDGNDLEEDFITWREQFWPAVCEHF-----GV	233
	*** ** * * . . *	
HsMTRR	LPVASPASLRDLDLVKSELLHIESQVELL--RFDDSGRKDSEVLKQNAVNS	214
CeMTRR	-AITESSNLKLNQVKTE----EEKKALLQKRIEDEESDDEGRGRVIGID-	206
HsCPR	EATGEESSIRQYEL-----VVHTDIDAAKVYMGEMGRKLSYEN	271
	
HsMTRR	NQSNVVIEDF---ESSLTRSVPLS-QASLNIPGLPPEYLQVHLQESLGQ	260
CeMTRR	---MLIPEHYDYPEISLLKGSQTLSDENLRVPIAPQPFIVSSVSNRKLP	253
HsCPR	QKP-----PFD-----AKNPFLAAVTTNRKLN	293
	
HsMTRR	EESQVS-----VTSADPVFQVPISKAVQLTT--NDAIKTTLLVELDIS	301
CeMTRR	EDTKLEWQNLCKMPGVVTKPFEVLVVSAEFVTDPFSSKIKTKRMITVDFG	303
HsCPR	QGTE-----RHLMHLELD	306
	
HsMTRR	N--TDFSYQPGDAFSVICPNSDSEVQSLQRL--LQLEDKREHCVLLKIKAD	348
CeMTRR	DHAAELQYEPGDAIYFCVPNPALVNFILKRCGVLDIADQOCEL-SINPK	352
HsCPR	ISDSKIRYESGDHVAVYPANDSALVNQLGK--ILGADLD--VVMSSLNNL	351
	. * . ** * * . . *	
HsMTRR	TKKKGATLPQHIPAGCSLQFIFTWCLEIRAI PKKAFLRALVDYTSDSA EK	398
CeMTRR	TEKINAQIPGHVHKITTLRHMTTCLDIRRAPGRPLIRVLAESTSDPNEK	402
HsCPR	DEESNKKHP--FPCPTSYRTALTYLDITNPPRTNVLYELAQYASEPSEQ	399
	* * * * * . * *	

Fig. 4-3

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HsMTRR	RRLQEL--CSKQGAADYSRFVRDACACLLDLLLAFSPCQPPLSLLLEHLP	446
CeMTRR	RRLLEL--CSAQGMKDFTFVTRTPGLSLADMLFAFPNVKPPVDRLELLP	450
HsCPR	ELLRKMASSSGEGKELYLSWVVEARRHILAILQDCPSLRPPIDHLCCELLP	449
	* . * . * . . * . * * . * * *	
	FAD FAD FAD	
HsMTRR	KLQPRPYSCASSSLFHPGKLHVFVNIVEFLSTATTEVLRKGVCTGWLALL	496
CeMTRR	RLIPRPYSMSS---YENRKARLIYSEMEFPATDGRRHRSRKGLATDWLNSL	497
HsCPR	RLQARYYSIASSSKVHPNSVHICAVVVEYETKAGR--INKGVATNWL---	494
	. * * * * . * . . * . * * *	
HsMTRR	VASVLQPNIHASHEDSGKALAPKISISPRTTNSFHLP-----DDPSIP	539
CeMTRR	R-----IGDKVQVLGKEPARFRLPPLGMTKNSAGKLP	529
HsCPR	RAKE-----PVGENGGRALVPMFVRKSQFRLPFK-----ATTP	527
	. * *	
	NADPH	
HsMTRR	IIMVGPGTGIAPFIGFLOHREKLQEHPDGNFGAMW-LFFGCRHKDRDYL	588
CeMTRR	LLMVGPGTGVSVFLSFLHFLRKLKQDSPSDFVDVPRVLFFGCRDSSVDAI	579
HsCPR	VIMVGPGTGVAPFIGFIQERAWLRQQGKE--VGETLLYYGCRRSDEDYL	574
	..*****.. * . * . * . . * . * . *	
	NADPH NADPH	
HsMTRR	FRKELRHFLKHGILTHLKVFSRDAPVGEEAPAKYVQDNIQLHGQOVAR	638
CeMTRR	YMSELEMFVSEGILTDLIICESEQ-----KGERVQDGLRKYLDKVLP	621
HsCPR	YREELAQFHRDGALTQLNVAFSRE-----QSHKVYVQHLLKQDREHLWK	618
	. ** * * * * . * * *	
	NADPH	
HsMTRR	ILLQE-NGHIYVCGDAKNMAKDVEDALVQIISKEVGVEKLEAMKTLATLK	687
CeMTRR	FLTASTESKIFICGDAKGMSKDVWQCFSDIVASDQGIPLDLEAKKKLMDLK	671
HsCPR	LI--EGGAHIYVCGDARNMARDVQNTFYDIVAELGAMEHAQAVDYIKKLM	666
	. . * . * . * . * . * . . * . . *	
	NADPH/FAD	
HsMTRR	EEKRYLQDIWS	698
CeMTRR	KSDQYIEDVWG	682
HsCPR	TKGRYSLDVWS	677
	* * *	

Fig. 4-4

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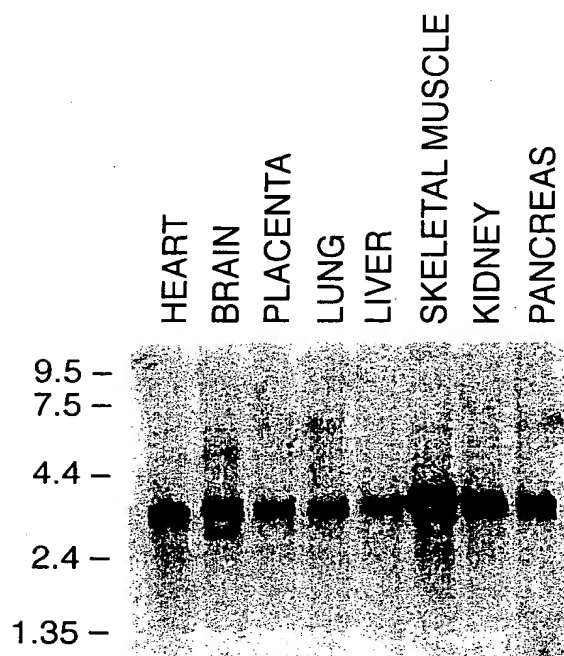


Fig. 5A



Fig. 5B

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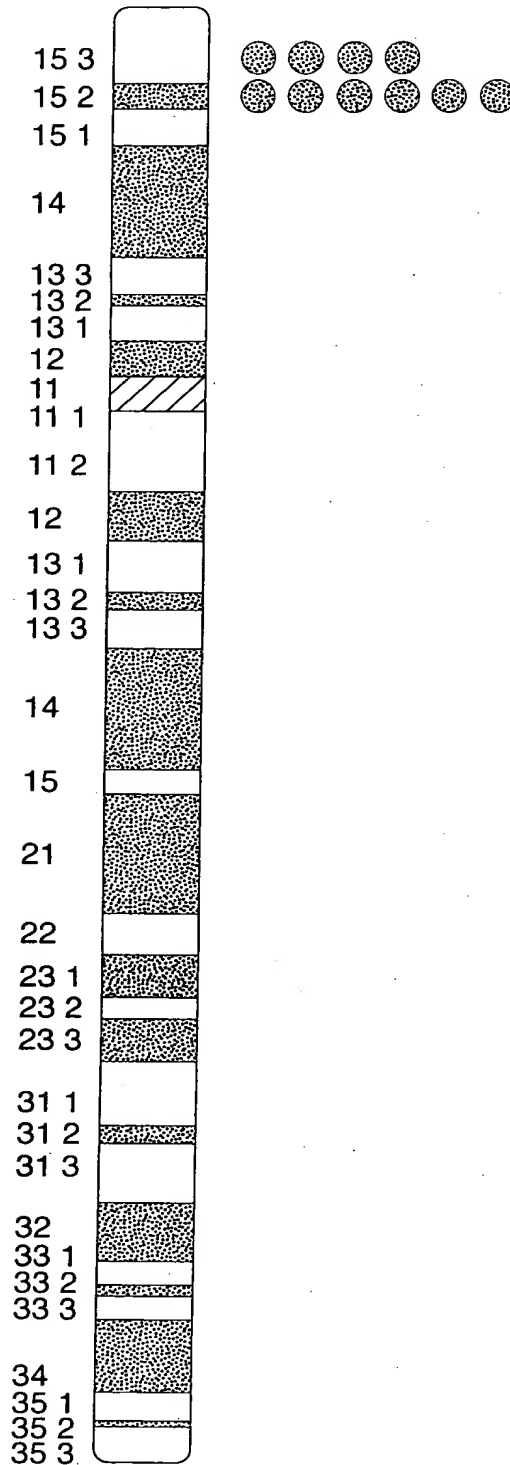


Fig. 6

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Fig. 7A

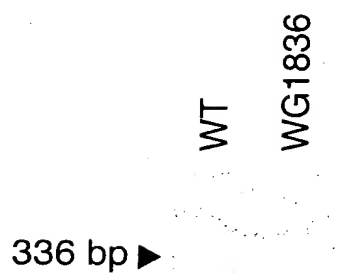


Fig. 7B

Position	Sequence	Accession#	Protein	Organism
572	GAMW [▲] FFGCRHKDRDYLF	(AF025794)	MTRR	(H sapiens)
558	GETLLYYGCRRSDEDYLY	(A60557)	CPR	(H sapiens)
559	GETLLYYGCRRAAEDYLY	(D00101)	CPR	(O cuniculus)
560	GESILYFGCRKRSEDYIY	(X93090)	CPR	(D melanogaster)
572	GPALLFFGCRNRQMDFIY	(P37116)	CPR	(V radiata)
573	GPTVLFFGCRKSDEDFLY	(Z26938)	CPR	(A niger)
1281	CPMVLVFGCRQSKIDHIY	(D16408)	NOS I	(H sapiens)
1009	GRMTLVFGCRRPDEDHIY	(U05810)	NOS II	(H sapiens)
1040	TPMTLVFGCRCSQLDHLY	(L26914)	NOS III	(H sapiens)
380	GRMTLVFGCRHPPEEDHLY	(U85094)	NOS	(O cuniculus)
1005	GDMILLFGCRHPDMDHIY	(U46504)	NOS	(G gallus)
481	GKNWLFFGNPHFTEDFLY	(M23008)	SR	(E coli)
915	GEVFLYLGSRHKREEYLY	(L26503)	SR	(S cerevisiae)
407	GRNWLIFGNRHFHRDFLY	(Z23169)	SR	(T roseopersicina)
261	GLAWLFLGVANVDSLLYD	(X99419)	FNR	(P sativum)
251	GLAWLFLGVPTSSSLLYK	(P00455)	FNR	(S oleracea)

Fig. 7C

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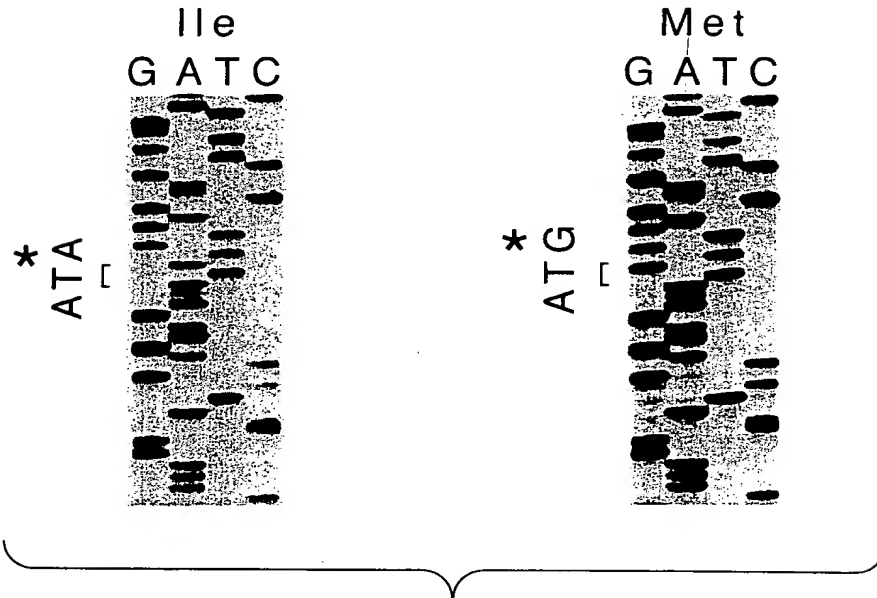


Fig. 8A

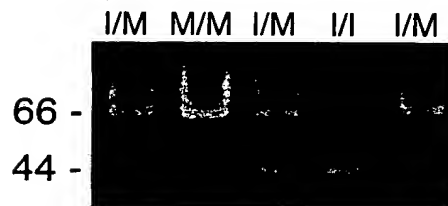


Fig. 8B